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MAJOR ARTICLE

Value and Clinical Impact of an Infectious Disease-Supervised Outpatient Parenteral Antibiotic Therapy Program

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Background. Outpatient parenteral antibiotic therapy (OPAT) is a safe and effective modality for treating serious infections. This study was undertaken to define the value of OPAT in a multicentered infectious disease (ID) private practice setting.

Methods. Over a period of 32 months, 6120 patients were treated using 19 outpatient ID offices in 6 states. Analysis included patient demographics, indications of OPAT, diagnoses, therapeutic agent, duration of therapy, and site of therapy initiation. Outcomes were stratified by therapeutic success, clinical relapse, therapeutic complications, and hospitalizations after initiating therapy. Statistical analysis included an ordinal logistic regression analysis.

Results. Forty-three percent of patients initiated therapy in an outpatient office, and 57% began therapy in a hospital. Most common diagnoses treated were bone and joint (32.2%), abscesses (18.8%), cellulitis (18.5%), and urinary tract infection (10.8%). Ninety-four percent of patients were successfully treated, and only 3% were hospitalized after beginning therapy. Most common cause of treatment failure was a relapse of primary infection (60%), progression of primary infection (21%), and therapeutic complication (19%).

Conclusions. An ID-supervised OPAT program is safe, efficient, and clinically effective. By maximizing the delivery of outpatient care, OPAT provides a tangible value to hospitals, payers, and patients. This program is a distinctive competency available to ID physicians who offer this service to patients.

Keywords. ID private practice; ID value; OPAT.

Outpatient parenteral antimicrobial therapy (OPAT) for the treatment of infectious diseases (IDs) was first described in the United States in 1974 [1] and has experienced significant growth. As healthcare expenditures have continued to rise, OPAT has been positioned as an alternative cost-effective vehicle to treat serious IDs. The primary goal of an OPAT program is to allow patients to complete treatment safely and effectively in the comfort of their home or another outpatient site. Secondary goals include maintaining a normality of lifestyle, avoiding the expense of hospitalization, and the exposure to nosocomial pathogens [2]. An organized and effectively managed OPAT program is a valuable asset to physicians, hospitals, payers, and most importantly patients [3, 4].

Numerous studies have delineated the utility of OPAT to successfully treat patients with cellulitis, osteomyelitis, septic arthritis, bacteremia, infected prosthetic joints, and pyelonephritis [5–12]. In addition, OPAT has also been found to be effective in virtually all segments of the population [1, 13, 14] and in multiple practice settings including private practice, traditional academic programs, and a Veterans Affairs medical center [11, 14, 15].

Successful therapy with OPAT encompasses complex processes that must be coordinated and managed. In an ideal setting, a diagnosis must be secured, a causative organism should be identified, and a narrow-spectrum antimicrobial agent should be chosen. Afterwards, the criteria for OPAT must be reviewed, the patient and attending physician should be informed of therapeutic recommendations, intravenous access should be secured, resources should be delineated, and an appropriate model for OPAT should be chosen. Barriers to effective OPAT include the following: ambiguous diagnoses, multidrug-resistant organisms (MDROs), oral agents available but not well tolerated, social constraints, lack of transportation, limited resources, and drug allergies.

The aim of this study was to define the utility, efficacy, safety, and patient benefits available through the usage of OPAT in a multicentered ID private practice setting.

METHODS

Outpatient Parenteral Antibiotic Therapy Program

Metro Infectious Disease Consultants (MIDC) is a fully integrated ID private practice, including 75 ID physicians.

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Outpatient parenteral antimicrobial therapy is available in each of 19 offices located in Illinois, Iowa, Indiana, Arizona, Michigan, and Alabama. Patients were admitted into the program from August 2011 to December 2014. Informed consent was deemed unnecessary because all data were deidentified before the analysis. Before admission, all patients were seen in consultation with an MIDC ID physician, where the diagnosis and indication for OPAT were verified. The consultations occurred both in the (1) hospital, hospital initiated (HI) and (2) MIDC outpatient offices, office initiated (OI). Patients received infusion therapy either in a MIDC office or in their homes. All patients were evaluated at initiation of OPAT and every 1–2 weeks depending on patient stability and diagnosis.

Venous access was obtained either in a hospital before discharge or in the MIDC offices. Peripheral intravenous catheters were used for infusions of 10 days or less, whereas midline or peripherally inserted central catheters were reserved for more prolonged therapeutic courses.

Infusion therapy was delivered through various models, including in-office infusion where patients received infusions and nursing care in one of the MIDC offices. All other patients received their infusion therapy at home through either the Teach and Train (TT) or Home Infusion Therapy (HIT) model [16]. In the HIT model, the patient received all infusion therapy as well as nursing care at home. In the TT model, infusions were administered at home, but nursing care was delivered in the MIDC office. Models were selected based on diagnosis, clinical stability, available resources, and patient preference.

The program was coordinated by a clinical pharmacist in conjunction with the MIDC medical director. Data collected included diagnosis, indication for OPAT, duration of therapy, consecutive and sequential therapies, site of therapy initiation, patient comorbidities, adverse drug reactions (ADRs), *Clostridium difficile* infections, intravenous access complications, and clinical outcomes. Weekly laboratory studies were obtained in accordance with published guidelines and included complete blood count, serum creatinine, liver enzymes, and drug levels or serum creatine phosphokinase, when indicated [2].

Patients were excluded from the analysis if they received less than 3 days of OPAT. Primary therapy was the initial antimicrobial agent prescribed for the individual patients. Concurrent therapy was defined as receipt of a second antimicrobial agent added to the primary therapy. Sequential therapy was defined as use of an antimicrobial agent prescribed after discontinuing the primary therapy.

Outcomes were recorded as success, modified success, or failure. Success was defined as (1) cure of the infection without relapse within 30 days of therapy completion or (2) admission to the hospital due to progression of their primary infection or for a therapeutic complication. Modified success was defined as cure of the infection but with a therapeutic complication such as an ADR or a line-related complication, but without a hospital admission. Line-related complications included mechanical disruption, inadvertent removal, or infection. Failure was defined as a relapse of the primary infection within 30 days of therapy completion or hospitalization due to progression of primary infection or treatment complication. Data was collected through a retrospective chart review of MIDC outpatient records.

Statistical Analysis

Treatment outcome was measured using an ordinal variable, coded such that "0" = Failure (n = 350; 5.7%), "1" = Modified Success (n = 139; 2.3%) and "2" = Success (n = 5631; 92%). Treatments were administered to match each patient's unique diagnostic situation, leading to variation in treatment duration, concurrent therapies, and treatment sequences. The effect of the duration of the first therapy, presence of a concurrent therapy, presence of 1 sequential therapy, and presence of 2 sequential therapies on outcomes were assessed using a series of ordinal logistic regression models. We conducted a test of parallel lines for each model to ensure that the proportional odds assumption had not been violated. First, the effects of the independent variables on treatment outcome were considered individually. Next, effects of covariates such as age (mean = 59.38, standard deviation = 15.93), gender (43.9% female), and diabetic status (22% had diabetes listed as a diagnosis) were assessed individually. Finally, significant independent variables were assessed together in a more comprehensive model that included selected covariates. Descriptive statistics were computed for all relevant study variables (see Table 1).

A more comprehensive ordinal logistic regression model was used to test the relative effects of primary therapy duration, presence of concurrent therapy, presence of 1 sequential therapy, and presence of 2 sequential therapies on treatment outcomes. The model was also constructed to account for the

Table 1. Clinical Data

Presence of concurrent treatment	863	14.1%
Presence of 1 sequential therapy	605	9.9%
Presence of 2 sequential therapies	55	0.9%
Diagnosis Group		
Bone/joint	1970	32.2%
Abscess	1149	18.8%
Cellulitis	1135	18.5%
Urinary tract infection	659	10.8%
Bacteremia	400	6.5%
Other	807	13.2%
Primary therapy		
Ertapenem	1390	22.7%
Ceftriaxone	1288	21%
Daptomycin	1189	19.4%
Vancomycin	1144	18.7%
Cefazolin	345	5.6%
Cefepime	245	4%
Other	519	8.5%

potential effects of important patient characteristics including age, gender, and diabetes.

RESULTS

A total of 6120 patients were enrolled in the program from August 2011 to December 2014. Patient demographic data, site of infusion initiation, infusion model, and treatment outcome are delineated in Tables 2 and 3. Forty-three percent of patients were enrolled in the program through the OI arm, having not been previously admitted to the hospital. Fifty-seven percent of patients were enrolled in the program after a hospital admission, the HI arm. Most patients received infusion therapy in their homes through either the TT or HIT models. Patients in the OI arm of the program had similar outcomes: 94.3% cure of the primary infection and a 2.5% hospital admission rate (Table 4).

The most common causes of treatment failures were relapse within 30 days of the primary infection, followed by progression of primary infection and a therapeutic complication requiring a hospital admission (Table 5). Most patients received 1 antimicrobial agent in a single therapeutic course. Fourteen percent received concurrent therapy, and another 10% received sequential therapy. The most common diagnosis for OPAT was a bone or joint infection, which also resulted in the most prolonged duration of therapy (Table 6). Primary therapies largely consisted of agents that could be used on a daily basis, which eased the burden of administration.

All patients were given a primary therapy regimen (N = 6120). Presence of concurrent therapy was significantly associated with lower odds of treatment success (Slope [b] = −0.29; standard error [SE] = 0.13; $P = .019$). Among those who had a concurrent therapy (n = 863; 14.1%), duration of concurrent therapy was not significantly associated with treatment outcomes ($b = 0.011$; SE = 0.008; $P = .174$).

Table 2. Patient Demographics

Total patients enrolled in program	6120
Gender	
Male	3489 (57%)
Female	2631 (43%)
Age	
Range	2–100 y/o (avg. 59)
0–18	80 (1.3%)
19–64	3580 (58.5%)
65+	2460 (40.2%)
Diabetes	1345 (22%)
Initiation site of therapy	
Office	2604 (42.5%)
Hospital	3516 (57.5%)
Infusion model	
IOI	2754 (45%)
Home	3366 (55%)

Abbreviations: avg., average; IOI, in-office infusion.

Table 3. Patient Outcomes

Success	5631 (92%)
Modified success	139 (2.3%)
Failures	350 (5.7%)
Patients hospitalized after entering program	161 (2.6%)

Presence of at least 1 sequential therapy (n = 605; 9.9%) was significantly associated with lower odds of treatment success (b = −1.45; SE = 0.11; $P < .001$). Approximately 1% of patients were given a second therapy sequence (n = 55; 0.9%). Presence of 2 sequential therapies was significantly associated with lower odds of treatment success (b = −1.62; SE = 0.30; $P < .001$).

Neither age (b = 0.0003; SE = 0.003; $P = .907$) nor gender (b = −0.09; SE = 0.10; $P = .366$) was significantly associated with treatment outcomes. However, patients with diabetes (n = 1345; 22%) had lower odds of treatment success than patients without diabetes (b = −0.26; SE = 0.11; $P = .015$). Adjusting for all of the above-mentioned variables, the presence of at least 1 sequential therapy was significantly associated with lower odds of treatment success (b = −1.37; SE = 0.12; $P < .001$). None of the other variables in the more comprehensive model showed statistical significance.

DISCUSSION

The data presented, to the best of our knowledge, represents the first ID private practice multicentered OPAT study. Over a period of 32 months, a large cohort of patients were treated for commonly encountered IDs, using 19 MIDC offices in 6 states. Outcomes were adjudicated using predefined criteria, and over 94% of patients were treated successfully, regardless of the therapy initiation site. As such, these results may be generalized to large segments of the population and any ID-supervised OPAT program.

A more rigorous definition of failure was used in this study, incorporating hospitalization due to progression of primary infection or treatment complication. Nevertheless, less than 6% of patients failed and only 3% were admitted to a hospital after beginning therapy. Previous studies have reported much higher rates of readmission, but they included all causes of hospitalization. However, approximately 70% of readmissions were infection related [17–19]. This study was not designed to predict which patients may be likely to succeed or fail therapy.

Table 4. Patients Admitted to the Program Through the Office-Initiated Arm

Total patients enrolled in the office-initiated arm	2604 (43%)
Success	2396 (92%)
Modified success	60 (2.3%)
Failures	148 (5.7%)
Patients hospitalized after entering program	65 (2.5%)

Table 5. Patients That Failed Therapy

Total patients that failed therapy	350 (5.7%)
Relapse of primary infection within 30 d	210 (60%)
Primary infection progression	74 (21%)
Therapeutic complication	66 (19%)

However, the presence of diabetes and concurrent or sequential therapies increased the likelihood that the primary therapeutic course would fail. The latter findings suggest the possibility of reverse causality. Patients with poorer outcomes during or after the initial regimen may have been, by definition, a select group in which failure could have been predicted. The other possibility is that the additional or amended therapies were necessary due to a delay in diagnosis, therapeutic complication, or payer constraints that were unreported. Further study is necessary to define this issue and utilize the data to generate a predictive model for OPAT success.

Our study has several weaknesses. The retrospective nature of the data collection may have resulted in unrecorded readmissions, ADRs, or secondary infections. In addition, a selection bias was operative in that some patients did not qualify for OPAT based on lack of resources, family dynamics, or transportation availability. Several comorbidities such as peripheral vascular disease and smoking were not formally assessed. Observer bias may also have occurred because the principal ID physician initially adjudicated the outcome status. However, the lack of clinical relapses suggests that this was infrequent. Finally, the success rate for bone and joint infections may be overstated because clinical relapses may occur long after the initial course of therapy is completed. Patients classified as modified success were not hospitalized but experienced a line complication, ADRs, or secondary infection such as *C difficile*. Although line complications were tracked compulsively, ADRs are historically underreported and, unless the reaction mandated a change of therapy, may have gone unnoticed. In addition, *C difficile* infections may have been empirically treated by other non-MIDC physicians, not come to our attention, and therefore not recorded.

The changes in healthcare continue to value outpatient options for care. Hospital-based infusion centers typically charge a facility fee, escalating the cost of care without demonstrably increasing the value to patients, families, or payers [16, 20, 21]. Accordingly, some payers have begun to mandate that infusion services be delivered in a nonhospital-based site of care [22, 23]. In addition, the Centers for Medicare & Medicaid Services has begun to financially penalize institutions for unnecessary or repeat admissions [24]. The data presented illustrates that an ID-supervised OPAT program obviates the above issues. As an effective and efficient model for outpatient infusion services, patients receive infusion therapy at home or in a physician's office, while minimizing the likelihood of serious complications including hospital admission and exposure to MDROs.

Table 6. Average Duration of Therapy

Diagnosis	Days
Bone/joint	37.6
Abscess	27.5
Bacteremia	22.5
Pneumonia	21.6
UTI	12.6
Cellulitis	12.4

Abbreviations: UTI, urinary tract infection.

We recommend that future studies use the same rigorous criteria for outcomes assessment used here. Hospitalizations and readmissions should be delineated by relapse or progression of primary infection or therapeutic complication. A prediction model of OPAT success should be studied using patient comorbidities, resources, access to transportation, and family support. These data would then be used to stratify patients into the appropriate transition of care model.

Finally, the financial impact of an outpatient program that efficiently delivers successful therapy to patients previously treated in the inpatient arena cannot be overstated. Forty-three percent of patients were begun on OPAT without a preceding hospitalization. If we conservatively assume that a hospitalization with at least a 3-day length of stay was avoided for each of these patients, then 7896 hospital days were saved. In addition, the availability of an OPAT program should decrease an inpatient stay by at least 1 day, saving an additional 3489 days. Depending on the institutional cost structure, this may have saved between 9 and 12 million dollars. This does not take into account the number of hospital-acquired infections and lack of patient satisfaction that may have been encountered.

CONCLUSIONS

Recent studies have articulated the value of an ID physician in the inpatient arena [25]. However, the medical climate continues to dictate the preferential use of outpatient programs to accomplish what has historically been delivered in an inpatient venue. Infectious disease specialists that organize, manage, and effectively deliver OPAT will continue to successfully interact with hospital systems, payers, accountable care organizations, and other physician organizations. By providing a tangible value to an infected patient population, OPAT serves as a distinctive competency: the ability to manage and direct a complicated patient's care in multiple forums.

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References

1. Rucker RW, Harrison GM. Outpatient intravenous medications in the management of cystic fibrosis. Pediatrics **1974**; 54:358–60.
2. Tice AD, Rehm SJ, Dalovisio JR, et al. Practice guidelines for outpatient parenteral antimicrobial therapy. IDSA guidelines. Clin Infect Dis **2004**; 38:358–60.
3. Paladino JA, Poretz D. Outpatient parenteral antimicrobial therapy today. Clin Infect Dis **2010**; 51(Suppl 2):S198–208.
4. Petrak RM, Allison GM. An overview of OPAT. In: Shah A, Norris A, eds. Handbook of Outpatient Parenteral Antimicrobial Therapy for Infectious Diseases. 3rd ed. Tarrytown, NY: CRG Publishing; **2016**.
5. Antoniskis A, Anderson BC, van Volkinburg EJ, et al. Feasibility of outpatient self-administration of parenteral antibiotics. West J Med **1978**; 128:203–6.
6. Kind AC, Williams DN, Persons G, Gibson JA. Intravenous antibiotic therapy at home. Arch Intern Med **1979**; 139:413–5.
7. Poretz DM, Eron LJ, Goldenberg RI, et al. Intravenous antibiotic therapy in an outpatient setting. JAMA **1982**; 248:336–9.
8. Rehm SJ, Weinstein AJ. Home intravenous antibiotic therapy: a team approach. Ann Intern Med **1983**; 99:388–92.
9. Balinsky W, Nesbitt S. Cost-effectiveness of outpatient parenteral antibiotics; a review of the literature. Am J Med **1989**; 87:301–5.
10. Tice AD. An office model of outpatient parenteral antibiotic therapy. Rev Infect Dis **1991**; 13(Suppl 2):S184–8.
11. Poretz DM. Evolution of outpatient parenteral antibiotic therapy. Infect Dis Clin North Am **1998**; 12:827–34.
12. Skorodin N, Petrak R, Fliegelman R, Hines D. Clinical effectiveness of an ID supervised outpatient parenteral antibiotic therapy program. Presented at the 4th Annual ID Week. San Diego, CA, October 10, 2015. Abstract: 1453.
13. Petrak RM. Outpatient antibiotic therapy in long-term care facilities. Infect Dis Clin North Am **1998**; 12:995–1008.
14. Cox AM, Malani PN, Wiseman SW, Kauffman CA. Home intravenous antimicrobial infusion therapy; a viable option in older adults. J Am Geriatr Soc **2007**; 55:645–50.
15. Nguyen JJ. Hospitalist to home: outpatient perenteral antimicrobial therapy at an academic center. Clin Infect Dis **2010**; 51(Suppl 2):S220–3.
16. McKinsey DS, Petrak RM. Models of OPAT. In: Shah A, Norris A, eds. Handbook of Outpatient Parenteral Antimicrobial Therapy for Infectious Diseases. 3rd ed. Tarrytown, NY: CRG Publishing; **2016**.
17. Allison GM, Muldoon EG, Kent DM, et al. Prediction model for 30-day hospital readmissions among patients discharged receiving outpatient parenteral antibiotic therapy. Clin Infect Dis **2014**; 58:812–9.
18. Means L, Gross AE, Sikka M, Bleasdale S. Predictors of hospital readmission in patients receiving outpatient parenteral antimicrobial therapy (OPAT). Presented at the 3rd Annual ID Week. Philadelphia, PA. October 11, 2014. Abstract 1298.
19. Alvarado F, Metzger B, Mandel RM, et al. Low hospital admission rates following physician office infusion center (POIC)-based outpatient treatment with intravenous antibiotics (IVABs). Presented at the 3rd Annual ID Week. Philadelphia, PA. October 10, 2014. Abstract 763.
20. Huff C. Facility fees pressure physicians to talk costs with patients. Medical Economics. **December 15, 2014**:1–4.
21. Worth T. Hospital facility fees: why cost may give independent physicians and edge. Medical Economics. **August 12, 2014**:1–6.
22. United Healthcare letter to providers. Site of service prior authorization requirement. **July 1, 2015**:1–3.
23. BlueCross BlueShield letter to providers. Update to medication benefit change. **July 6, 2015**:1–2.
24. Readmissions reduction program 2014. Centers for Medicare & Medicaid Services. Available at: https://www.cms.gov/medicare/medicare-fee-for-service-payment/acuteinpatientpps/readmissions-reduction-program.html. Accessed 3 September 2016.
25. Schmitt S, McQuillen DP, Nahass R, et al. Infectious diseases specialty intervention is associated with decreased mortality and costs. Clin Infect Dis **2014**; 58:22–8.